



# STIC Search Report

## Biotech-Chem Library

STIC Database Tracking Number: 12798

**TO:** Ben Sackey  
**Location:** rem/5b31/5c18  
**Art Unit:** 1626  
**Monday, July 26, 2004**

**Case Serial Number:** 10/618044

**From:** Noble Jarrell  
**Location:** Biotech-Chem Library  
**Rem 1B71**  
**Phone:** 272-2556

**Noble.jarrell@uspto.gov**

### Search Notes

**SEARCH REQUEST FORM****Scientific and Technical Information Center**

Requester's Full Name: BEN JACKY Examiner #: 73489 Date: 7/26/04  
 Art Unit: 1626 Phone Number 302-0704 Serial Number: 101618,044  
 Mail Box and Bldg/Room Location: REM 5B31 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

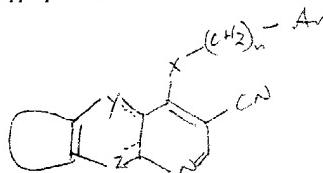
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Tricyclic Protein Kinase Inhibitors

Inventors (please provide full names): Dan M. Berger et al.

Earliest Priority Filing Date: \_\_\_\_\_

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

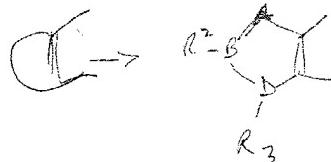


Elected Species is  
 $8-(4\text{-chloro-5-methoxy-2-methylphenyl})-3-[2-(4\text{-methyl-1-}\text{methyl})\text{ethyl}-3\text{H-imidazo[4,5-g]quinoxine-7-carbo-}\text{nitrile}$

Ar is phenyl substituted

n is -O-

X is NH



A, D are N or A, B and D are N

<b>STAFF USE ONLY</b>		<b>Type of Search</b>	<b>Vendors and cost where applicable</b>
Searcher:	<u>Noble</u>	NA Sequence (#)	STN <u>639</u>
Searcher Phone #:		AA Sequence (#)	Dialog
Searcher Location:		Structure (#)	<u>2</u> Questel/Orbit
Date Searcher Picked Up:	<u>7/26/04</u>	Bibliographic	Dr.Link
Date Completed:	<u>7/26/04</u>	Litigation	Lexis/Nexis
Searcher Prep & Review Time:	<u>30</u>	Fulltext	Sequence Systems
Clerical Prep Time:		Patent Family	WWW/Internet
Online Time:	<u>30</u>	Other	Other (specify)

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(FILE 'HOME' ENTERED AT 08:57:21 ON 26 JUL 2004)

L1 FILE 'HCAPLUS' ENTERED AT 08:57:30 ON 26 JUL 2004  
1 US2004110762/PN

FILE 'REGISTRY' ENTERED AT 08:57:45 ON 26 JUL 2004

L2 FILE 'HCAPLUS' ENTERED AT 08:57:50 ON 26 JUL 2004  
TRA L1 1- RN : 291 TERMS

L3 FILE 'REGISTRY' ENTERED AT 08:57:51 ON 26 JUL 2004  
291 SEA D2

FILE 'REGISTRY' ENTERED AT 08:57:54 ON 26 JUL 2004

L4 FILE 'REGISTRY' ENTERED AT 08:57:56 ON 26 JUL 2004  
1 US2004110762/PN

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FILE COVERS 1907 - 26 Jul 2004 VOL 141 ISS 5  
FILE LAST UPDATED: 25 Jul 2004 (20040725/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

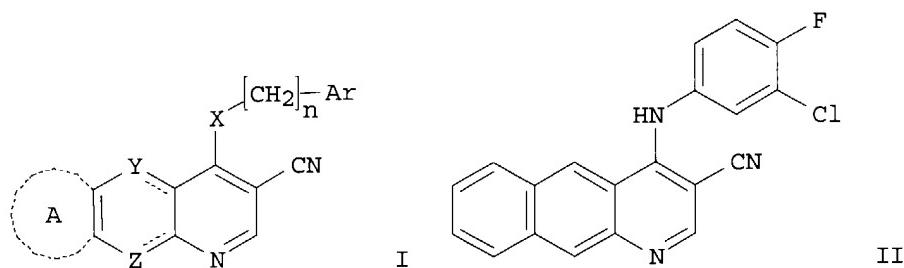
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L1 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2001:906207 HCAPLUS  
DN 136:37618  
ED Entered STN: 16 Dec 2001  
TI Preparation of substituted aromatic tricyclic compounds containing nicotinonitrile rings as protein kinase inhibitors  
IN Berger, Dan M.; Dutia, Minu D.; Demorin, Frenel F.; Boschelli, Diane H.; Powell, Dennis W.; Tsou, Hwei-ru; Wissner, Allan; Zhang, Nan; Ye, Fei; Wu, Biqi  
PA American Home Products Corporation, USA; Wyeth  
SO U.S. Pat. Appl. Publ., 107 pp.  
CODEN: USXXCO  
DT Patent

LA English  
IC ICM A61K031-5377  
ICS A61K031-496; A61K031-4738; C07D491-02  
NCL 514232800  
CC 28-13 (Heterocyclic Compounds (More Than One Hetero Atom))  
Section cross-reference(s): 1

FAN.CNT 1		KIND	DATE	APPLICATION NO.	DATE
	PATENT NO.				
PI	US 2001051620 US 6638929 <b>US 20041710762</b>	A1 B2 <b>A1</b>	20011213 20031028 <b>20040810</b>	US 2000-751274	20001229
PRAI	US 1999-240905P US 2000-751274	P A3	19991229 20001229	US 2003-618044	20030710 <--
OS	MARPAT 136:37618				
GI					



AB The title compds. I [Ar = (un)substituted cycloalkyl, pyridyl, pyrimidinyl, etc.; n = 0-1; X = NH, O, S, NR; R = alkyl; Y, Z = both carbon or N; A = (un)substituted benzo, pyrido, pyrimido, etc.] which are useful as inhibitors of protein tyrosine kinase and are antiproliferative agents, were prepared E.g., a 3-step synthesis of II which showed IC<sub>50</sub> of 0.005 .mu.M against EGF-R kinase (recombinant enzyme), was given.

ST arom tricyclic compd prepn protein kinase inhibitor; EGF receptor kinase inhibitor arom tricyclic compd prepn; antitumor arom tricyclic compd prepn; KDR kinase inhibitor arom tricyclic compd prepn; mitogen activated protein kinase inhibitor arom tricyclic compd prepn; src kinase inhibitor arom tricyclic compd prepn

IT Antitumor agents  
(preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile)

IT 79079-06-4, EGF receptor kinase 139691-76-2, Raf kinase 141349-89-5,  
Src kinase 142243-02-5, Mitogen activated protein kinase 150977-45-0  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(preparation of substituted aromatic tricyclic compds. containing

(preparation of substituted aromatic heterocyclic compounds containing  
nicotinonitrile  
rings as protein kinase inhibitors)

IT	263149-40-2P	348617-29-8P	348617-39-0P	348617-40-3P	348617-42-5P
	348617-43-6P	348617-45-8P	348617-60-7P	348617-61-8P	348617-63-0P
	348617-64-1P	348617-89-0P	348617-94-7P	348617-95-8P	348618-04-2P
	348618-05-3P	348618-16-6P	348618-17-7P	348618-18-8P	348618-33-7P
	348618-34-8P	348618-37-1P	348618-38-2P	348618-46-2P	348618-50-8P
	348618-53-1P	348618-56-4P	348618-57-5P	348618-59-7P	348618-64-4P
	348618-65-5P	348618-81-5P	348619-28-3P		

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(preparation of substituted aromatic tricyclic compds. containing nicotinonitrile

rings as protein kinase inhibitors)

IT	348617-17-4P	348617-19-6P	348617-20-9P	348617-26-5P	348617-27-6P
	348617-28-7P	348617-30-1P	348617-38-9P	348617-41-4P	348617-44-7P
	348617-46-9P	348617-47-0P	348617-50-5P	348617-51-6P	348617-52-7P
	348617-54-9P	348617-55-0P	348617-56-1P	348617-58-3P	348617-59-4P
	348617-62-9P	348617-65-2P	348617-66-3P	348617-71-0P	348617-72-1P
	348617-75-4P	348617-79-8P	348617-80-1P	348617-81-2P	348617-82-3P
	348617-83-4P	348617-84-5P	348617-85-6P	348617-90-3P	348617-98-1P
	348617-99-2P	348618-00-8P	348618-01-9P	348618-02-0P	348618-03-1P
	348618-06-4P	348618-07-5P	348618-19-9P	348618-20-2P	348618-35-9P
	348618-36-0P	348618-39-3P	348618-40-6P	348618-41-7P	348618-42-8P
	348618-43-9P	348618-44-0P	348618-47-3P	348618-58-6P	348618-60-0P
	348618-61-1P	348618-62-2P	348618-63-3P	348618-66-6P	348618-67-7P
	348618-68-8P	348618-74-6P	348618-82-6P	348618-83-7P	348618-84-8P
	348618-85-9P	348618-86-0P	348618-87-1P	348618-88-2P	348618-89-3P
	348618-90-6P	348618-91-7P	348618-92-8P	348618-93-9P	348618-94-0P
	348618-95-1P	348618-96-2P	348618-97-3P	348618-98-4P	348618-99-5P
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	348619-10-3P	348619-11-4P	348619-12-5P	348619-13-6P	348619-14-7P
	348619-15-8P	348619-16-9P	348619-17-0P	348619-18-1P	348619-19-2P
	348619-20-5P	348619-21-6P	348619-22-7P	348619-23-8P	348619-24-9P
	348619-25-0P	348619-26-1P	348619-27-2P	348619-29-4P	

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted aromatic tricyclic compds. containing nicotinonitrile

rings as protein kinase inhibitors)

IT	79-10-7, Acrylic acid, reactions 90-05-1, Guaiacol 94-05-3, Ethyl (ethoxymethylene)cyanoacetate 105-34-0, Methyl cyanoacetate 108-01-0, 2-(Dimethylamino)ethanol 109-01-3, 1-Methylpiperazine 110-91-8, Morpholine, reactions 139-59-3, 4-Phenoxyaniline 288-36-8, 1H-1,2,3-Triazole 348-62-9, 4-Chloro-2-fluorophenol 367-21-5, 3-Chloro-4-fluoroaniline 504-88-1, 3-Nitropropionic acid 540-88-5, tert-Butyl acetate 554-00-7, 2,4-Dichloroaniline 591-19-5, 3-Bromoaniline 622-40-2, 4-(2-Hydroxyethyl)morpholine 632-02-0, 3-Chloropropyl p-toluenesulfonate 814-68-6, Acryloyl chloride 873-38-1, 2-Bromo-4-chloroaniline 882-33-7, Phenyl disulfide 1142-19-4, 4,4'-Dichlorodiphenyl disulfide 2038-03-1, 4-(2-Aminoethyl)morpholine 2835-95-2, 5-Amino-o-cresol 4637-24-5 5335-29-5, 3-Chloro-4-phenoxyaniline 5959-52-4, 3-Amino-2-naphthoic acid 20357-25-9, 6-Nitroveratraldehyde 24313-88-0, 3,4,5-Trimethoxyaniline 33693-48-0, 4-Benzylxy-3-methoxybenzyl alcohol 34674-75-4 35212-85-2, Methyl 3-aminobenzo[b]thiophene-2-carboxylate 39786-35-1, Ethyl 3-amino-2-benzo[b]furancarboxylate 43073-44-5, 6,7-Dimethoxy-2,3-naphthalenedicarboxylic anhydride 50868-72-9, 5-Methoxy-2-methylaniline 57946-56-2, 4-Chloro-2-fluoroaniline 59404-86-3, 4-Benzylxy-3-chloroaniline 59922-33-7 62492-42-6 63224-35-1 76513-69-4, 2-(Trimethylsilyl)ethoxymethyl chloride 76878-17-6 85006-21-9, 2-Chloro-5-methoxyaniline hydrochloride 98404-04-7, 2-Chloro-4-fluoro-5-methoxyaniline 98446-49-2, 2,4-Dichloro-5-methoxyaniline 131775-97-8 133088-44-5 133303-88-5 204915-71-9, 4-(2-Chloroethoxy)-3-methoxybenzaldehyde 348619-47-6				
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RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile  
rings as protein kinase inhibitors)

IT	3590-37-2P, Ethyl 3-nitropropionate	53544-07-3P	53815-60-4P		
	222622-96-0P	263149-39-9P	309269-57-6P	348617-15-2P	348617-16-3P
	348617-21-0P	348617-22-1P	348617-23-2P	348617-24-3P	348617-25-4P
	348617-31-2P	348617-32-3P	348617-33-4P	348617-34-5P	348617-35-6P
	348617-36-7P	348617-37-8P	348617-48-1P	348617-49-2P	348617-57-2P
	348617-67-4P	348617-68-5P	348617-69-6P	348617-70-9P	348617-73-2P
	348617-74-3P	348617-76-5P	348617-77-6P	348617-78-7P	348617-86-7P
	348617-87-8P	348617-88-9P	348617-91-4P	348617-92-5P	348617-93-6P
	348617-96-9P	348617-97-0P	348618-08-6P	348618-09-7P	348618-10-0P
	348618-11-1P	348618-12-2P	348618-13-3P	348618-14-4P	348618-15-5P
	348618-21-3P	348618-22-4P	348618-23-5P	348618-24-6P	348618-25-7P
	348618-26-8P	348618-27-9P	348618-28-0P	348618-29-1P	348618-30-4P
	348618-31-5P	348618-32-6P	348618-45-1P	348618-48-4P	348618-49-5P
	348618-51-9P	348618-52-0P	348618-54-2P	348618-55-3P	348618-69-9P
	348618-70-2P	348618-71-3P	348618-72-4P	348618-73-5P	348618-75-7P
	348618-76-8P	348618-77-9P	348618-78-0P	348618-79-1P	348618-80-4P
	348619-30-7P	348619-31-8P	348619-32-9P	348619-33-0P	348619-34-1P
	348619-35-2P	348619-36-3P	348619-37-4P	348619-38-5P	348619-39-6P
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	348619-45-4P	348619-46-5P			

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile  
rings as protein kinase inhibitors)

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FILE LAST UPDATED: 23 JUL 2004 <20040723/UP>  
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L4 ANSWER 1 OF 1 WPIX COPYRIGHT 2004 THOMSON DERWENT on STN  
AN 2001-522007 [57] WPIX  
DNC C2001-155768  
**TM** New tricyclic heterocycles are protein kinase inhibitors, useful in the treatment, inhibition and eradication of neoplasms, polycystic kidney disease and colonic polyps.  
 DC B02  
**IN** BERGER, D M; BOSCHELLI, D H; DEMORIN, F F; DUTIA, M D; POWELL, D W; TSOU, H; WISSNER, A; WU, B; YE, F; ZHANG, N  
 PA (AMHP) AMERICAN HOME PROD CORP; (AMHP) WYETH; (AMHP) WYETH INC  
 CYC 95  
 PI WO 2001047892 A1 20010705 (200157)\* EN 377 C07D215-54  
     RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ  
     NL OA PT SD SE SL SZ TR TZ UG ZW  
     W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM  
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 JP 2003519127 W 20030617 (200349) 341 C07D221-08  
 US 6638929 B2 20031028 (200372)\*# A61K031-535  
 CN 1437584 A 20030820 (200374) C07D215-54  
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 20001229; US 2001051620 A1 Provisional US 1999-240905P 19991229, US  
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 20001229, US 2003-618044 20030710  
 FDT AU 2001024646 A Based on WO 2001047892; EP 1242382 A1 Based on WO  
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 on WO 2001047892; US 2004110762 A1 Div ex US 6638929  
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 US 2003-618044 20030710  
 IC ICM A61K031-506; A61K031-535; A61K031-5377; C07D215-54; C07D221-08  
 ICS A61K031-429; A61K031-435; A61K031-4353; A61K031-4355; A61K031-4365;  
 A61K031-4375; A61K031-473; A61K031-4738; A61K031-4745; A61K031-496;  
 A61K031-498; A61K031-4985; A61P001-00; A61P003-10; A61P005-14;  
 A61P009-00; A61P009-10; A61P011-00; A61P013-12; A61P017-00;  
 A61P017-06; A61P017-14; A61P019-02; A61P025-00; A61P029-00;  
 A61P031-04; A61P031-12; A61P035-00; A61P037-06; A61P037-08;  
 A61P043-00; C07C205-59; C07C229-70; C07D279-12; C07D307-85;  
 C07D333-70; C07D401-10; C07D401-12; C07D401-14; C07D471-02;  
 C07D471-04; C07D487-02; C07D491-02; C07D491-04; C07D491-048;  
 C07D495-04; C07D513-04

AB WO 200147892 A UPAB: 20011005

NOVELTY - Tricyclic heterocycles (I) are new.

DETAILED DESCRIPTION - Tricyclic heterocycles of formula (I) and their salts are new.

ring system = fused 5,6,6-tricycle, 6,6,6-tricycle, 6,5,6-tricycle, or 6,6,6-tricycle;

Ar = 3-7C cycloalkyl (optionally substituted by 1 or more 1-6C alkyl), or pyridinyl, pyrimidinyl or phenyl (all optionally substituted), 8-12 membered bicyclic aryl or bicyclic heteroaryl containing 1-4 N, O or S (both optionally substituted), or -A'-T-L;

A' = pyridinyl, pyrimidinyl or phenyl (all optionally substituted);

T = -NH(CH<sub>2</sub>)<sub>m</sub>- , -O(CH<sub>2</sub>)<sub>m</sub>- , -S(CH<sub>2</sub>)<sub>m</sub>- , -NR(CH<sub>2</sub>)<sub>m</sub>- , -(CH<sub>2</sub>)<sub>m</sub>- , -(CH<sub>2</sub>)<sub>m</sub>NH- , -(CH<sub>2</sub>)<sub>m</sub>O- , -(CH<sub>2</sub>)<sub>m</sub>S- , -SO(CH<sub>2</sub>)<sub>m</sub>- , SO<sub>2</sub>(CH<sub>2</sub>)<sub>m</sub>- , -CO(CH<sub>2</sub>)<sub>m</sub>- , -(CH<sub>2</sub>)<sub>m</sub>CO- , -(CH<sub>2</sub>)<sub>m</sub>SO- , -(CH<sub>2</sub>)<sub>m</sub>SO<sub>2</sub>- or -(CH<sub>2</sub>)<sub>m</sub>NR- ;

L = phenyl (optionally substituted), or 5-6 membered heteroaryl ring containing 1-3 N, O or S and optionally substituted;

m = 0-3;

n = 0-1;

X = NH, O, S or NR;

R = 1-6C alkyl;

Y, Z = C or N; or

Y = N, O or S; and

Z = bond; or

Y = bond; and

Z = N, O or S;

ring A = a group of formula (a)-(l);

B = C or N;

D, E = C, N, O or S;

dotted line = optional double bond;

R1-R4 = absent, H, OH, halo, amino, hydroxyamino, CF<sub>3</sub>, CF<sub>3</sub>O, SH, 1-6C alkyl, 3-8C cycloalkyl, 2-6C alkenyl, 2-6C alkynyl, 2-6C alkenyloxy, 2-6C

alkynyoxy, 1-6C hydroxyalkyl, 1-6C mercaptoalkyl, halomethyl, 2-7C alkoxymethyl, 1-6C alkoxy, 3-8C cycloalkoxy, 1-6C alkylthio, 3-8C

cycloalkylthio, 1-6C alkylsulfinyl, 1-6C alkylsulfonyl, 1-6C alkylsulfonamido, 2-6C alkenylsulfonamido, 2-6C alkynylsulfonamido, CN,

NO<sub>2</sub>, carboxy, 2-7C alkoxy carbonyl, 2-7C alkanoyl, 3-7C alkenoyl, 4-12C

N-alkyl-N-alkenylamino, 6-12C dialkenylamino, phenylamino, benzylamino, phenoxy, phenyl, thiophenoxy, benzyl, 1-6C alkylamino, 2-7C alkanoyloxy,

3-8C alkenoyloxy, 3-8C alkynoyloxy, carbamoyl, 2-7C N-alkylcarbamoyl, 3-13C N,N-dialkylcarbamoyl, 2-12C dialkylamino, 2-7C alkanoyloxy methyl,

2-7C alkenoyloxy methyl, 2-7C alkynoyloxy methyl, azido, benzoyl, 2-7C carboxyalkyl, 3-8C carboxyalkoxyalkyl, R8R9-CH-M-(C(R6)2)k-X-,

R7-(C(R6)2)g-X-, R7-(C(R6)2)p-M-(C(R6)2)k-X-, Het-(C(R6)2)q-W-(C(R6)2)k-X-, Ph-(C(R6)2)q-W-(C(R6)2)k-X-, R5-CONH(CH<sub>2</sub>)q-, R5-C equivalent toC-CONH(CH<sub>2</sub>)q-, (R5)2C=C(CN)(CH<sub>2</sub>)q-, (R5)2C=C(R5)CONH(CH<sub>2</sub>)q-,(R5)2C=C(R5)SO<sub>2</sub>NH(CH<sub>2</sub>)q-, R5OC(O)NH(CH<sub>2</sub>)q-, R5NHC(O)NH(CH<sub>2</sub>)q-,(R5)2NC(O)NH(CH<sub>2</sub>)q-, R5HNC(O)O(CH<sub>2</sub>)q-, R5HNC(S)NH(CH<sub>2</sub>)q-,(R5)2NC(S)NH(CH<sub>2</sub>)q-, (R5)2NC(O)O(CH<sub>2</sub>)q-, or a group of formula (m) or (n);

R5 = H, 1-6C alkyl, 1-6C aminoalkyl, 2-9C N-alkylaminoalkyl, 3-12C

N,N-dialkylaminoalkyl, 4-12C N-cycloalkylaminoalkyl, 5-18C

N-cycloalkyl-N-alkylaminoalkyl, 7-18C N,N-dicycloalkylaminoalkyl,

morpholino-N-(1-6C alkyl), piperidino-N-(1-6C alkyl), N-(1-6C

alkyl)-piperazino-N-(1-6C alkyl), 3-11C azacycloalkyl-N-alkyl, 1-6C

hydroxyalkyl, 2-8C alkoxyalkyl or phenyl;

X = (CH<sub>2</sub>)<sub>m</sub>, O, S or NR6;

R7 = N(R6)2, OR6, J, N(R6)3+ or NR6(OR6);

M = NR6, O, S, N-((C(R6)2)pN(R6)2) or N-((C(R6)2)p-OR6);

W = NR6, O, S or bond;

Het = morpholine, thiomorpholine, thiomorpholine-S-oxide, thiomorpholine-S,S-dioxide, piperidine, pyrrolidine, aziridine, pyridine,

imidazole, 1,2,3-triazole, 1,2,4-triazole, thiazole, thiazolidine, tetrazole, piperazine, furan, thiophene, tetrahydrothiophene, tetrahydrofuran, dioxane, 1,3-dioxolane pyrrole or tetrahydropyran (all optionally C-substituted, and optionally N-substituted by 1-2 NR<sub>6</sub>);  
 Ph = optionally substituted phenyl;  
 R<sub>6</sub> = H, 1-6C alkyl, 2-6C alkenyl, 2-6C alkynyl, 1-6C cycloalkyl, 2-7C alkanoyl, 2-7C carbamoylalkyl, 1-6C hydroxyalkyl, 3-6C hydroxycycloalkyl or 2-7C carboxyalkyl, or optionally substituted phenyl;  
 R<sub>8</sub>, R<sub>9</sub> = N-((C(R<sub>6</sub>)<sub>2</sub>)pN(R<sub>6</sub>)<sub>2</sub>) or N-((C(R<sub>6</sub>)<sub>2</sub>)p-OR<sub>6</sub>);  
 J = H, Cl, F or Br;  
 g = 1-6;  
 k = 0-4;  
 p = 2-4;  
 q = 0-4;  
 r = 1-4; and  
 s = 1-6;  
 provided that:

(1) when ring A = group (1), at least 1 bond between E and B or B and D is a double bond; at least 1 of E, B or D is not C; only 1 of E, B or D = O or S; and the adjacent atoms to O or S are C;

(2) when R<sub>5</sub> is bound to an N atom, the resulting structures are not N-C-N or O-C-N radicals; and when R<sub>5</sub> is bound to an O atom, the resulting structure is not a -N-C-O- radical;

(3) when R<sub>6</sub> = 2-7C alkenyl or 2-7C alkynyl, the alkenyl and alkynyl moieties are bound to N or O through a saturated C atom in the alkenyl or alkynyl chain;

(4) when X = NR<sub>6</sub> and R<sub>7</sub> = N(R<sub>6</sub>)<sub>2</sub>, N(R<sub>6</sub>)<sub>3</sub>+ or NR<sub>6</sub>(OR<sub>6</sub>), then g = 2-6;

(5) when M = O or S and R<sub>7</sub> = OR<sub>6</sub>, then p = 1-4;

(6) when X = NR<sub>6</sub>, O or S, then k = 2-4;

(7) when X = O or S and M or W = O or S, then k = 1-4;

(8) when W is not a bond with Het bonded through an N atom, then q = 2-4; and

(9) when W = bond with Het bonded through an N atom and X = NR<sub>6</sub>, O or S, then k = 2-4.

An INDEPENDENT CLAIM is also included for the preparation of (I) via 14 different reaction pathways.

ACTIVITY - Cytostatic; Nephrotropic; Gastrointestinal; Hepatotropic; Dermatological.

MECHANISM OF ACTION - MAPK kinase inhibitor; RAF kinase inhibitor; SRC kinase inhibitor; ECK/LERK-1 kinase inhibitor; VEGF/KDR kinase inhibitor

In an assay to measure inhibition of cancer cell growth (see Skehan et. al., J. Natl. Canc. Inst., 82, 1107-1112 (1990)), 4-(2,4-dichloroanilino)-8-nitro(1)benzothieno(3,2-b)pyridine-3-carbonitrile (Ib) displayed IC<sub>50</sub> values of 0.46, 0.41, 0.59 and 0.67 micro g/ml against MDA-MB-435, A431, SK-BR3 and SW620 cell lines respectively.

USE - Compounds (I) are useful for treating, eradicating or inhibiting the growth of neoplasms, especially breast, kidney, bladder, mouth, larynx, esophagus, stomach, colon, ovary, lung, pancreas, liver, prostate and skin, and especially neoplasms that express EGFR or erbB2 (Her2). (I) are also useful in treating, eradicating or inhibiting polycystic kidney disease and colonic polyps, and for inhibiting the biological effects of a deregulated protein kinase (all claimed).

Dwg.0/0

FS	CPI
FA	AB; GI; DCN
MC	CPI: B05-B01B; B06-H; B10-B01A; B10-B02A; B10-G02; B14-D06; B14-H01B; B14-N10

Sackey 10/618044 Applicant

Page 8

=> b home  
FILE 'HOME' ENTERED AT 08:58:36 ON 26 JUL 2004

=>

=> b reg

**FILE: 'REGISTRY'** ENTERED AT 10:03:41 ON 26 JUL 2004  
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
 COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 JUL 2004 HIGHEST RN 715654-51-6  
 DICTIONARY FILE UPDATES: 23 JUL 2004 HIGHEST RN 715654-51-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

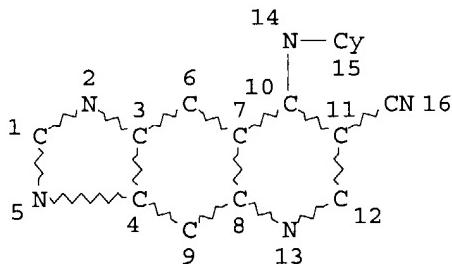
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

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L7 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

**L9 \* 20 SEA FILE=REGISTRY**

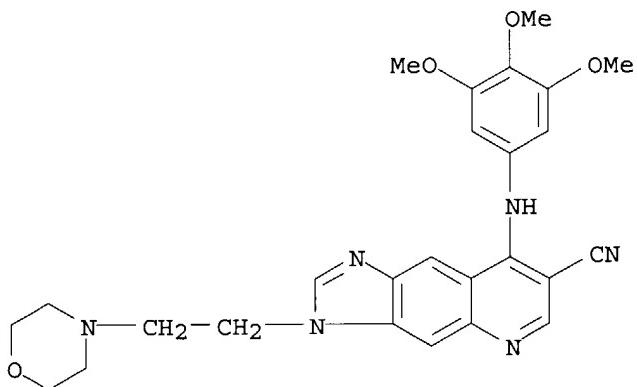
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**20 ANSWERS \***

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 CN 3H-Imidazo[4,5-g]quinoline-7-carbonitrile, 3-[2-(4-morpholinyl)ethyl]-8-[(3,4,5-trimethoxyphenyl)amino]- (9CI) (CA INDEX NAME)

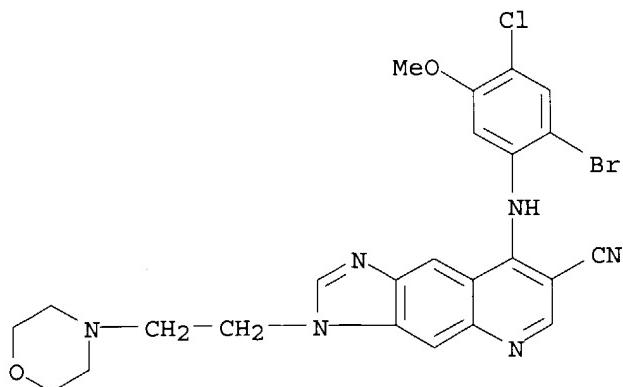
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 DT.CA CAplus document type: Journal  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

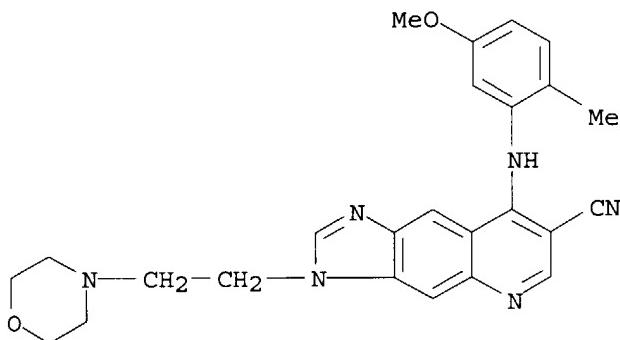
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 RN 500023-79-0 REGISTRY  
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 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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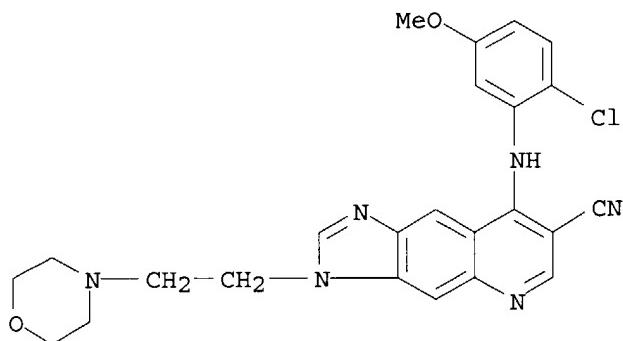
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 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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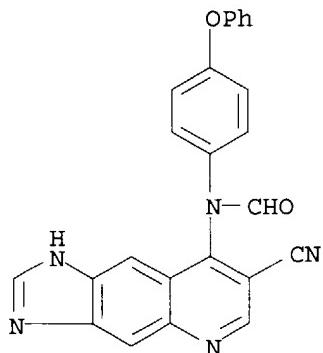
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 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 5 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 348619-42-1 REGISTRY  
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 DT.CA CAplus document type: Patent  
 RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



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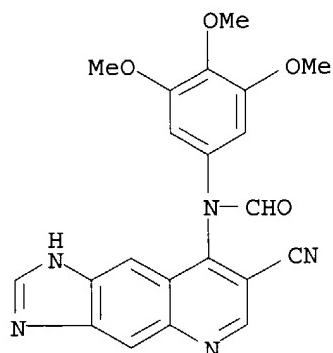
L9 ANSWER 6 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 348619-39-6 REGISTRY  
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 FS 3D CONCORD  
 MF C21 H17 N5 O4

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

DT.CA CAplus document type: Patent

RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)



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L9 ANSWER 7 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN

RN 348617-72-1 REGISTRY

CN 3H-Imidazo[4,5-g]quinoline-7-carbonitrile, 3-[2-(4-morpholinyl)ethyl]-8-[(4-phenoxyphenyl)amino]- (9CI) (CA INDEX NAME)

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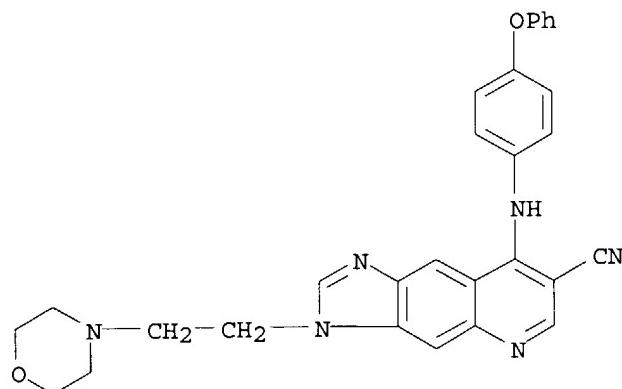
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LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL

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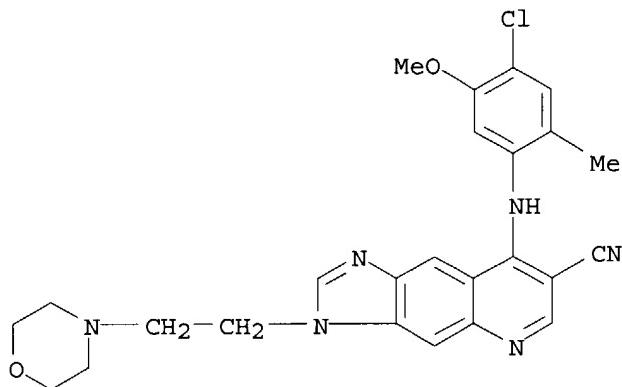


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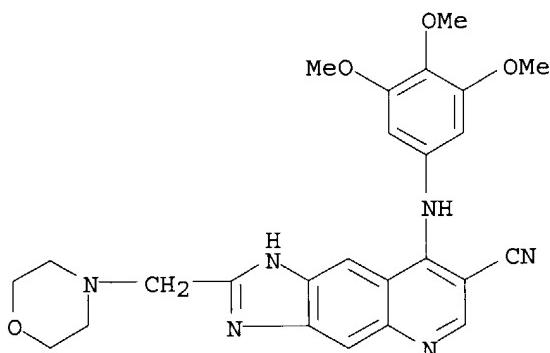
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 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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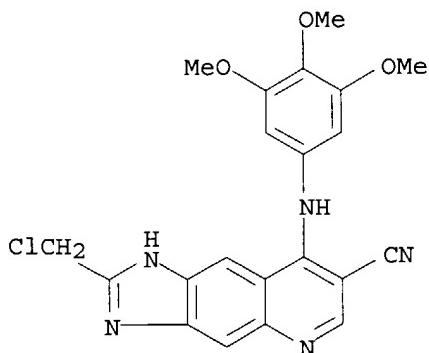
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 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



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L9 ANSWER 10 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN  
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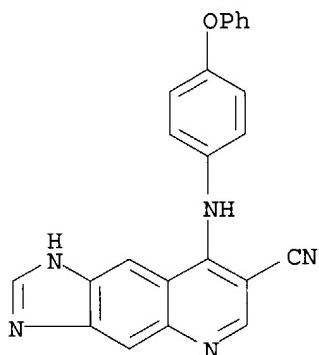


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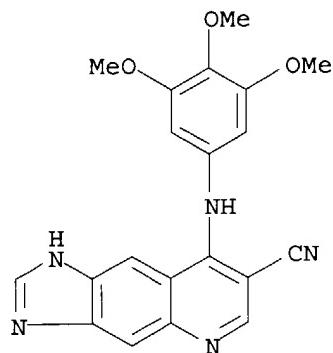
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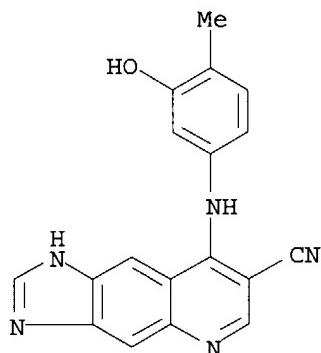
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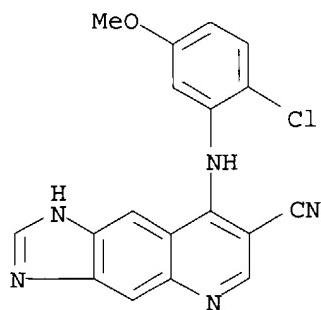
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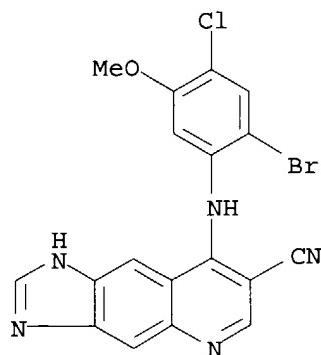
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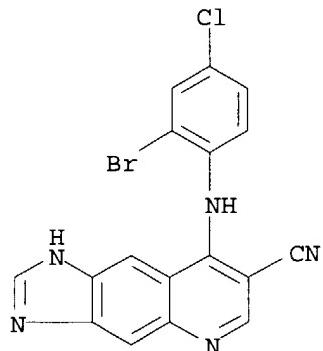


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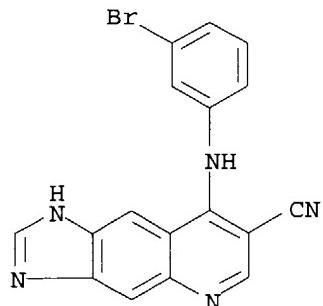
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 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL  
 DT.CA CAplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES  
     (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 17 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 348617-50-5 REGISTRY  
 CN 1H-Imidazo[4,5-g]quinoline-7-carbonitrile, 8-[(3-bromophenyl)amino]- (9CI)  
     (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C17 H10 Br N5  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL  
 DT.CA CAplus document type: Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES  
     (Uses)

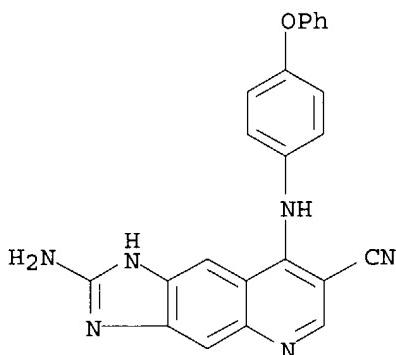


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)

## 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

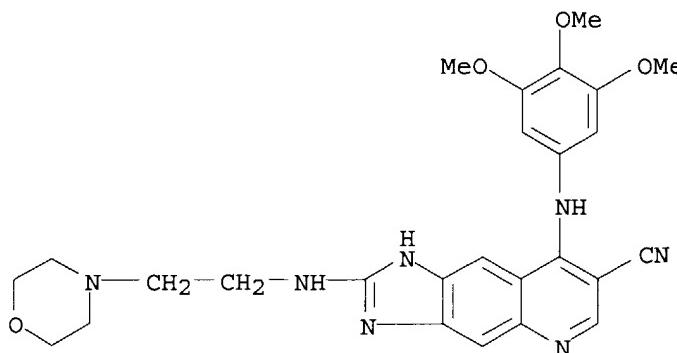
L9 ANSWER 18 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 348617-47-0 REGISTRY  
 CN 1H-Imidazo[4,5-g]quinoline-7-carbonitrile, 2-amino-8-[(4-phenoxyphenyl)amino]-, monohydrochloride (9CI) (CA INDEX NAME)  
 MF C23 H16 N6 O . Cl H  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPAT2, USPATFULL  
 DT.CA CAplus document type: Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



● HCl

2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

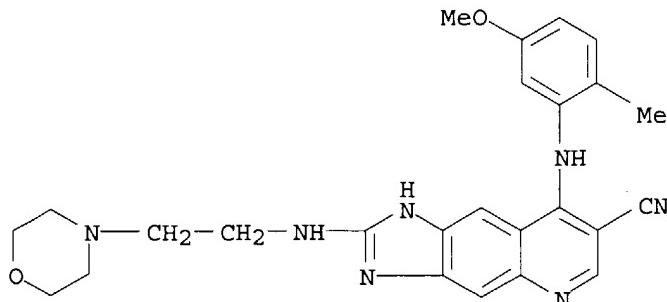
L9 ANSWER 19 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 348617-46-9 REGISTRY  
 CN 1H-Imidazo[4,5-g]quinoline-7-carbonitrile, 2-[[2-[(4-morpholinyl)ethyl]amino]-8-[(3,4,5-trimethoxyphenyl)amino]- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C26 H29 N7 O4  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL  
 DT.CA CAplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L9 ANSWER 20 OF 20 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 348617-44-7 REGISTRY  
 CN 1H-Imidazo[4,5-g]quinoline-7-carbonitrile, 8-[(5-methoxy-2-methylphenyl)amino]-2-[[2-(4-morpholinyl)ethyl]amino]- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C25 H27 N7 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER, USPAT2, USPATFULL  
 DT.CA CAplus document type: Journal; Patent  
 RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)  
 RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

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 1 US2004110762/PN

L2 FILE 'REGISTRY' ENTERED AT 08:57:45 ON 26 JUL 2004

L2 FILE 'HCAPLUS' ENTERED AT 08:57:50 ON 26 JUL 2004  
 TRA L1 1- RN : 291 TERMS

L3 FILE 'REGISTRY' ENTERED AT 08:57:51 ON 26 JUL 2004  
 291 SEA L2

L4 FILE 'REGISTRY' ENTERED AT 08:57:54 ON 26 JUL 2004

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 1 US2004110762/PN

L5 FILE 'REGISTRY' ENTERED AT 09:34:05 ON 26 JUL 2004  
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L7 STR L5

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 SAVE TEMP L9 SAC044FUL/A

L10 63 C25H25CLN602

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L15 3 L14 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)

L16 FILE 'HCAOLD' ENTERED AT 09:47:54 ON 26 JUL 2004  
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L17 FILE 'B' ENTERED AT 09:48:03 ON 26 JUL 2004  
 13 L7 FULL

L18 FILE 'MARPAT' ENTERED AT 09:48:44 ON 26 JUL 2004  
 STR L7

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L20 2 L18 FULL

L21 FILE 'HCAPLUS' ENTERED AT 09:50:50 ON 26 JUL 2004  
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L22 2 L21 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)

L23 FILE 'USPATFULL, USPAT2' ENTERED AT 09:51:12 ON 26 JUL 2004  
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L24 3 L23 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)

L25 FILE 'HCAOLD' ENTERED AT 09:51:49 ON 26 JUL 2004  
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L26 \* 2 L13 OR L22

FILE 'USPATFULL, USPAT2' ENTERED AT 09:52:38 ON 26 JUL 2004  
L27 3 L15 OR L24

FILE 'BEILSTEIN' ENTERED AT 09:59:59 ON 26 JUL 2004  
L28 0 L17 AND RN/FA

=> b hcap

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FILE COVERS 1907 - 26 Jul 2004 VOL 141 ISS 5  
FILE LAST UPDATED: 25 Jul 2004 (20040725/ED)

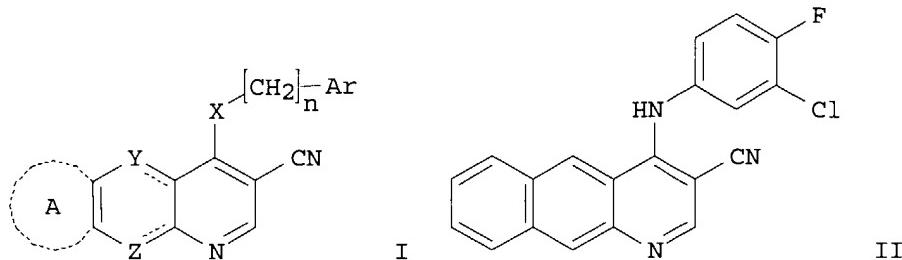
This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L26 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN  
AN 2001:906207 HCAPLUS  
DN 136:37618  
TI Preparation of substituted aromatic tricyclic compounds containing nicotinonitrile rings as protein kinase inhibitors  
IN Berger, Dan M.; Dutia, Minu D.; Demorin, Frenel F.; Boschelli, Diane H.; Powell, Dennis W.; Tsou, Hwei-ru; Wissner, Allan; Zhang, Nan; Ye, Fei; Wu, Biqi  
PA American Home Products Corporation, USA; Wyeth  
SO U.S. Pat. Appl. Publ., 107 pp.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001051620	A1	20011213	US 2000-751274	20001229 <--
	US 6638929	B2	20031028		
	US 2004110762	A1	20040610	US 2003-618044	20030710 <--
PRAI	US 1999-240905P	P	19991229 <--		
	US 2000-751274	A3	20001229		
OS	MARPAT	136:37618			
GI					



**AB** The title compds. I [Ar = (un)substituted cycloalkyl, pyridyl, pyrimidinyl, etc.; n = 0-1; X = NH, O, S, NR; R = alkyl; Y, Z = both carbon or N; A = (un)substituted benzo, pyrido, pyrimido, etc.] which are useful as inhibitors of protein tyrosine kinase and are antiproliferative agents, were prepared E.g., a 3-step synthesis of II which showed IC<sub>50</sub> of 0.005 .μ.M against EGF-R kinase (recombinant enzyme), was given.

**IT 348617-61-8P**

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of substituted aromatic tricyclic compds. containing

nicotinonitrile

rings as protein kinase inhibitors)

**IT 348617-44-7P 348617-46-9P 348617-47-0P**

**348617-50-5P 348617-51-6P 348617-52-7P**

**348617-54-9P 348617-55-0P 348617-56-1P**

**348617-58-3P 348617-62-9P 348617-71-0P**

**348617-72-1P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of substituted aromatic tricyclic compds. containing

nicotinonitrile

rings as protein kinase inhibitors)

**IT 348619-39-6P 348619-42-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation of substituted aromatic tricyclic compds. containing

nicotinonitrile

rings as protein kinase inhibitors)

**L26 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN**

**AN 2001:489374 HCAPLUS**

**DN 135:92639**

**\*TI Preparation of substituted aromatic tricyclic compounds containing nicotinonitrile rings as protein kinase inhibitors**

**\*IN Berger, Dan M.; Dutia, Minu D.; Demorin, Frenel F.; Boschelli, Diane H.; Powell, Dennis W.; Tsou, Hwei-ru; Wissner, Allan; Zhang, Nan; Ye, Fei; Wu, Biqi**

**PA American Home Products Corp., USA**

**SO PCT Int. Appl., 377 pp.**

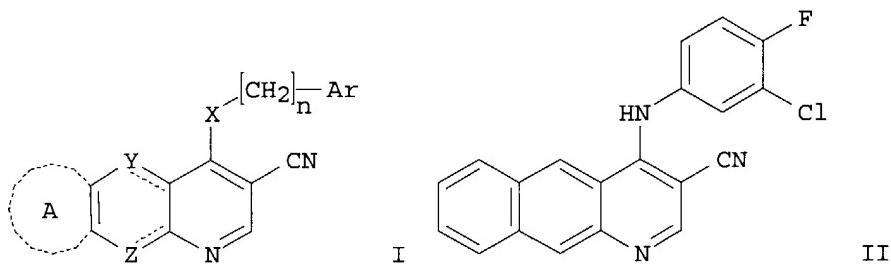
**CODEN: PIXXD2**

**DT Patent**

**LA English**

FAN.CNT 1

PATENT NO.		KIND	DATE	APPLICATION NO.		DATE
PI	WO 2001047892	A1	20010705	WO 2000-US35616	20001229	<--
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	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1242382	A1	20020925	EP 2000-988437	20001229	<--
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
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	JP 2003519127	T2	20030617	JP 2001-549364	20001229	<--
PRAI	US 1999-473600	A	19991229	<--		
	WO 2000-US35616	W	20001229			
OS	MARPAT 135:92639					
GI						



AB The title compds. I [Ar = (un)substituted cycloalkyl, pyridyl, pyrimidinyl, etc.; n = 0-1; X = NH, O, S, NR; R = alkyl; Y, Z = both carbon or N; A = (un)substituted benzo, pyrido, pyrimido, etc.] which are useful as inhibitors of protein tyrosine kinase and are antiproliferative agents, were prepared. E.g., a 3-step synthesis of II which showed IC<sub>50</sub> of 0.005 .mu.M against EGF-R kinase (recombinant enzyme), was given.

IT 348617-61-8P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(preparation of substituted aromatic tricyclic compds. containing

nicotinonitrile  
rings as protein kinase inhibitors)

IT 348617-44-7P 348617-46-9P 348617-47-0P  
348617-50-5P 348617-51-6P 348617-52-7P  
348617-54-9P 348617-55-0P 348617-56-1P  
348617-58-3P 348617-62-9P 348617-71-0P  
348617-72-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile

rings as protein kinase inhibitors)  
 IT 348619-39-6P 348619-42-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (preparation of substituted aromatic tricyclic compds. containing  
 nicotinonitrile  
 rings as protein kinase inhibitors)  
 RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

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 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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 CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitnum L27 tot

L27 ANSWER 1 OF 3 USPATFULL on STN  
 AN 2004:145089 USPATFULL  
 TI Tricyclic protein kinase inhibitors  
 IN Berger, Dan M., New City, NY, UNITED STATES  
 Dutia, Minu D., West Nyack, NY, UNITED STATES  
 DeMorin, Frenel F., Nanuet, NY, UNITED STATES  
 Boschelli, Diane H., New City, NY, UNITED STATES  
 Powell, Dennis W., Westchester, NY, UNITED STATES  
 Tsou, Hwei-Ru, New City, NY, UNITED STATES  
 Wissner, Allan, Ardsley, NY, UNITED STATES  
 Zhang, Nan, Eastchester, NY, UNITED STATES  
 Ye, Fei, Nanuet, NY, UNITED STATES  
 Wu, Biqi, Nanuet, NY, UNITED STATES  
 PA WYETH, Madison, NJ (U.S. corporation)  
 PI US 2004110762 A1 20040610  
 AI US 2003-618044 A1 20030710 (10)  
 RLI Division of Ser. No. US 2000-751274, filed on 29 Dec 2000, GRANTED, Pat.  
 No. US 6638929  
 PRAI US 1999-240905P 19991229 (60) <--  
 DT Utility  
 FS APPLICATION  
 LREP Anne M. Rosenblum, Esq., Suite 212, 163 Delaware Avenue, Delmar, NY,  
 12054  
 CLMN Number of Claims: 35  
 ECL Exemplary Claim: 1  
 DRWN No Drawings  
 LN.CNT 8418  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB This invention provides compounds of formula 1, having the structure  
 ##STR1##  
 which are useful as inhibitors of protein tyrosine kinase and are  
 antiproliferative agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 348617-61-8P  
 (preparation of substituted aromatic tricyclic compds. containing  
 nicotinonitrile  
 rings as protein kinase inhibitors)  
 IT 348617-44-7P 348617-46-9P 348617-47-0P

348617-50-5P 348617-51-6P 348617-52-7P  
 348617-54-9P 348617-55-0P 348617-56-1P  
 348617-58-3P 348617-62-9P 348617-71-0P  
 348617-72-1P

(preparation of substituted aromatic tricyclic compds. containing  
 nicotinonitrile  
 rings as protein kinase inhibitors)  
 IT 348619-39-6P 348619-42-1P  
 (preparation of substituted aromatic tricyclic compds. containing  
 nicotinonitrile  
 rings as protein kinase inhibitors)

L27 ANSWER 2 OF 3 USPATFULL on STN

AN 2001:229667 USPATFULL

TP Tricyclic protein kinase inhibitors  
 IN Berger, Dan M., New City, NY, United States  
 Dutia, Minu D., West Nyack, NY, United States  
 DeMorin, Frenel F., Nanuet, NY, United States  
 Boschelli, Diane H., New City, NY, United States  
 Powell, Dennis W., Westchester, NY, United States  
 Tsou, Hwei-Ru, New City, NY, United States  
 Wissner, Allan, Ardsley, NY, United States  
 Zhang, Nan, Eastchester, NY, United States  
 Ye, Fei, Nanuet, NY, United States  
 Wu, Biqi, Nanuet, NY, United States

PA American Home Products Corporation, Madison, NJ, United States,  
 07940-0874 (U.S. corporation)

PI US 2001051620 A1 20011213  
 US 6638929 B2 20031028

AI US 2000-751274 A1 20001229 (9)

PRAI US 1999-240905P 19991229 (60) <--

DT Utility

FS APPLICATION

LREP AMERICAN HOME PRODUCTS CORPORATION, PATENT SECTION, FIVE GIRALDA FARMS,  
 MADISON, NJ, 07940-0874

CLMN Number of Claims: 35

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 8432

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides compounds of formula 1, having the structure  
 ##STR1##

which are useful as inhibitors of protein tyro sine kinase and are  
 antiproliferative agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 348617-61-8P  
 (preparation of substituted aromatic tricyclic compds. containing  
 nicotinonitrile

rings as protein kinase inhibitors)

IT 348617-44-7P 348617-46-9P 348617-47-0P  
 348617-50-5P 348617-51-6P 348617-52-7P  
 348617-54-9P 348617-55-0P 348617-56-1P  
 348617-58-3P 348617-62-9P 348617-71-0P  
 348617-72-1P

(preparation of substituted aromatic tricyclic compds. containing  
 nicotinonitrile

rings as protein kinase inhibitors)

IT 348619-39-6P 348619-42-1P

(preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile  
rings as protein kinase inhibitors)

L27 ANSWER 3 OF 3 USPAT2 on STN  
 AN 2001:229667 USPAT2  
 TI Tricyclic protein kinase inhibitors  
 IN Berger, Dan M., New City, NY, United States  
 Dutia, Minu D., West Nyack, NY, United States  
 DeMorin, Frenel F., Nanuet, NY, United States  
 Boschelli, Diane H., New City, NY, United States  
 Powell, Dennis W., Westchester, NY, United States  
 Tsou, Hwei-Ru, New City, NY, United States  
 Wissner, Allan, Ardsley, NY, United States  
 Zhang, Nan, Eastchester, NY, United States  
 Ye, Fei, Nanuet, NY, United States  
 Wu, Biqi, Nanuet, NY, United States  
 PA Wyeth, Madison, NJ, United States (U.S. corporation)  
 PI US 6638929 B2 20031028  
 AI US 2000-751274 20001229 (9)  
 PRAI US 1999-240905P 19991229 (60) <--  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Solola, Taopiq; Assistant Examiner: Sackey, Ebenezer  
 LREP Hogan, Jr., John W.  
 CLMN Number of Claims: 16  
 ECL Exemplary Claim: 1  
 DRWN 0 Drawing Figure(s); 0 Drawing Page(s)  
 LN.CNT 7552  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB This invention provides compounds of formula 1, having the structure  
 ##STR1##  
 which are useful as inhibitors of protein tyrosine kinase and are  
 antiproliferative agents.  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 IT 348617-61-8P  
 (preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile  
rings as protein kinase inhibitors)  
 IT 348617-44-7P 348617-46-9P 348617-47-0P  
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 (preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile  
rings as protein kinase inhibitors)  
 IT 348619-39-6P 348619-42-1P  
 (preparation of substituted aromatic tricyclic compds. containing  
nicotinonitrile  
rings as protein kinase inhibitors)

=> b beilstein

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 FILE LAST UPDATED ON JUNE 15, 2004

FILE COVERS 1771 TO 2003.

\*\*\* FILE CONTAINS 8,997,153 SUBSTANCES \*\*\*

>>> PLEASE NOTE: Reaction data and substance data are stored in separate documents and can not be searched together in one query.

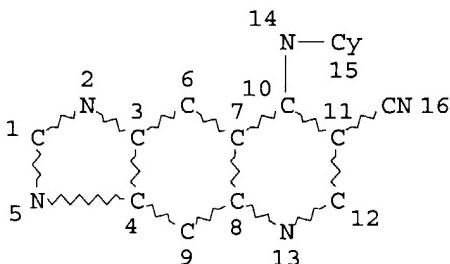
Reaction data for BEILSTEIN compounds may be displayed immediately with the display codes PRE (preparations) and REA (reactions). A substance answer set retrieved after the search for a chemical name, a molecular formula or a structure search for example can be restricted to compounds with available reaction information by concatenation with PRE/FA, REA/FA or more general with RX/FA. The BEILSTEIN Registry Number (BRN) is the link between a BEILSTEIN compound and belonging reactions. For more detailed reaction searches BRNs can be selected from substance answer sets and searched in the next step as reaction partner BRNs - Reactant (RX.RBRN) or Product BRN (RX.PBRN). After a search for reaction details substance documents associated with reactants or products may be retrieved by searching RX.PBRNs or RX.RBRNs as BRNs. <<<

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 \* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE, THESE \*  
 \* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. \*  
 \* FOR PRICE INFORMATION SEE HELP COST \*  
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L7 STR



NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

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 NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

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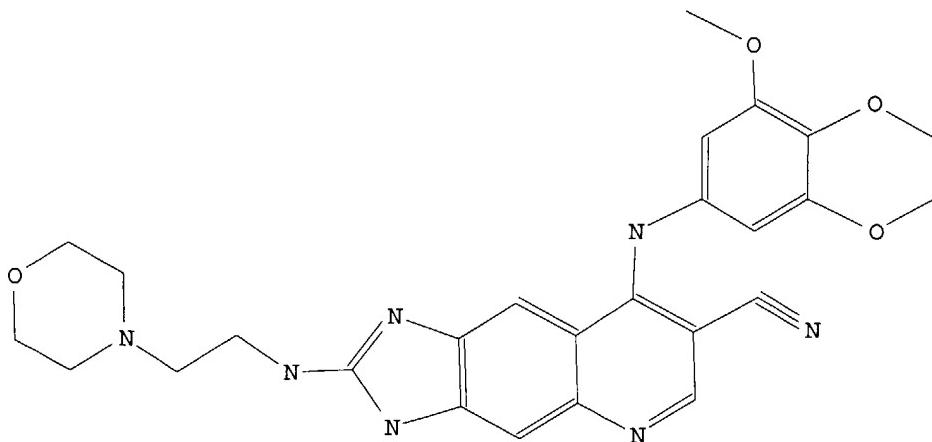
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13 ANSWERS

=&gt; d che ide exr l17 tot

L17 ANSWER 1 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9306940
Chemical Name (CN) :	2-(2-morpholin-4-yl-ethylamino)-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	2-(2-morpholin-4-yl-ethylamino)-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C <sub>26</sub> H <sub>29</sub> N <sub>7</sub> O <sub>4</sub>
Molecular Weight (MW) :	503.56
Lawson Number (LN) :	30824, 30356, 15326, 3018, 289
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7859336
Tautomer ID (TAUTID) :	8735609
Entry Date (DED) :	2003/04/17
Update Date (DUPD) :	2003/04/17



## Field Availability:

Code	Name	Occurrence
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BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
FS	File Segment	1

CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
====	=====	=====
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

Reaction:

RX

Reaction ID (.ID) :	9182059
Reactant BRN (.RBRN) :	9294295, 1210530
Reactant (.RCT) :	6,7-diamino-4-(3,4,5-trimethoxy-phenylamino)-quinoline-3-carbonitrile, 4-(2-isothiocyanato-ethyl)-morpholine
Product BRN (.PBRN) :	9306940
Product (.PRO) :	2-(2-morpholin-4-yl-ethylamino)-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
No. of React. Details (.NVAR) :	1

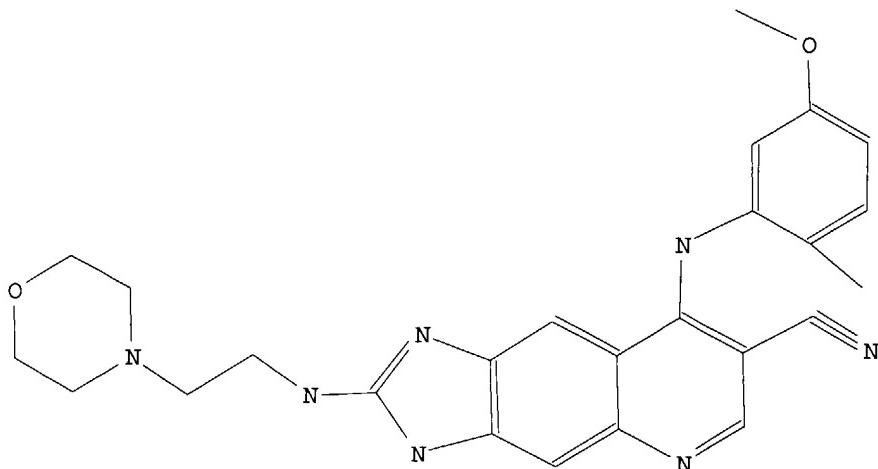
Reaction Details:

RX

Reaction RID (.RID) :	9182059.1
Reaction Classification (.CL) :	Multistage
Nr. of Stages (.SNR) :	2
Stage 1	
Stage 2	
Reagent (.RGT) :	HgO
Reference(s) :	
1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520	

L17 ANSWER 2 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9304845
Chemical Name (CN) :	8-(5-methoxy-2-methyl-phenylamino)-2-(2-morpholin-4-yl-ethylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	8-(5-methoxy-2-methyl-phenylamino)-2-(2-morpholin-4-yl-ethylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C25 H27 N7 O2
Molecular Weight (MW) :	457.53
Lawson Number (LN) :	30824, 30356, 14902, 3018, 289
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7857619
Tautomer ID (TAUTID) :	8734922
Entry Date (DED) :	2003/04/17
Update Date (DUPD) :	2003/04/17



## Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
<hr/>		
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

## Reaction:

RX

```

Reaction ID (.ID) : 9182058
Reactant BRN (.RBRN) : 9286834, 1210530
Reactant (.RCT) : 6,7-diamino-4-(5-methoxy-2-methyl-
phenylamino)-quinoline-3-carbonitrile,
4-(2-isothiocyanato-ethyl)-morpholine
Product BRN (.PBRN) : 9304845
Product (.PRO) : 8-(5-methoxy-2-methyl-phenylamino)-2-(2-
morpholin-4-yl-ethylamino)-3H-imidazo<4,5-
g>quinoline-7-carbonitrile
No. of React. Details (.NVAR) : 1

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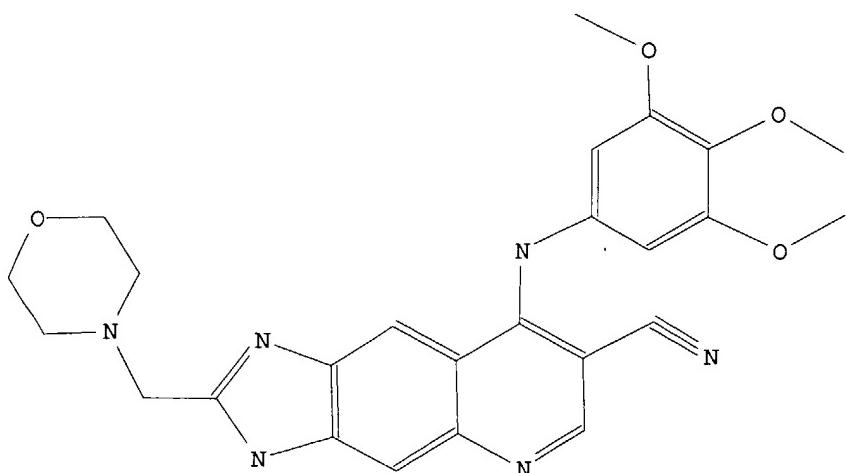
## Reaction Details:

RX

Reaction RID (.RID) : 9182058.1  
 Reaction Classification (.CL) : Multistage  
 Nr. of Stages (.SNR) : 2  
 Stage 1  
 Stage 2  
 Reagent (.RGT) : HgO  
 Reference(s) :  
 1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan;  
 DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank,  
 Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766;  
 BABS-6374520

L17 ANSWER 3 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) : 9304516  
 Chemical Name (CN) : 2-morpholin-4-ylmethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Autonom Name (AUN) : 2-morpholin-4-ylmethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Molec. Formula (MF) : C25 H26 N6 O4  
 Molecular Weight (MW) : 474.52  
 Lawson Number (LN) : 30824, 30357, 15326, 289  
 Compound Type (CTYPE) : heterocyclic  
 Constitution ID (CONSID) : 7857350  
 Tautomer ID (TAUTID) : 8733004  
 Entry Date (DED) : 2003/04/17  
 Update Date (DUPD) : 2003/04/17



Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	4
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
<hr/>		
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

Reaction:

RX

Reaction ID (.ID) : 9177041  
 Reactant BRN (.RBRN) : 9297462, 102549  
 Reactant (.RCT) : 2-chloromethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile, morpholine  
 Product BRN (.PBRN) : 9304516  
 Product (.PRO) : 2-morpholin-4-ylmethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 No. of React. Details (.NVAR) : 1

Reaction Details:

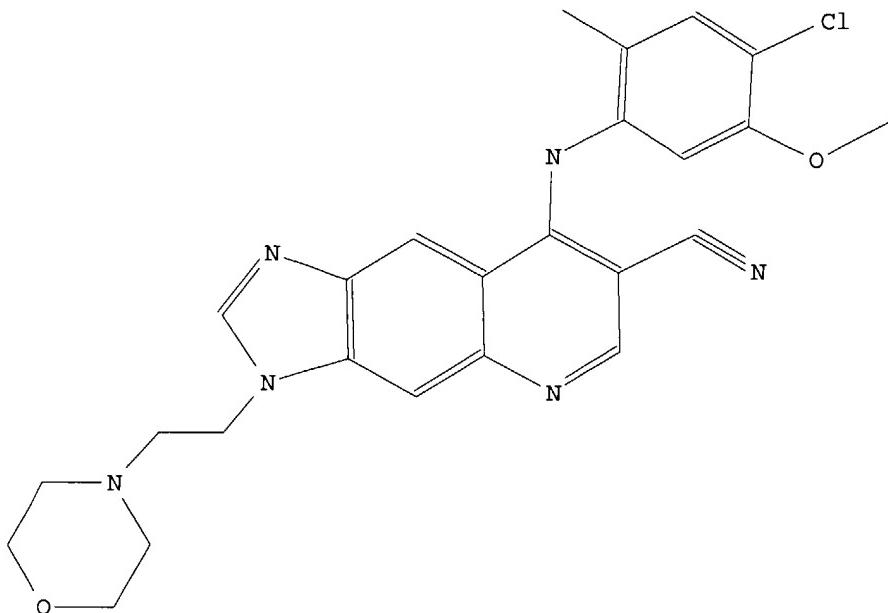
RX

Reaction RID (.RID) : 9177041.1  
 Reaction Classification (.CL) : Preparation  
 Reference(s) :  
 1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520

L17 ANSWER 4 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9303785
Chemical Name (CN) :	8-(4-chloro-5-methoxy-2-methyl-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	8-(4-chloro-5-methoxy-2-methyl-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C25 H25 Cl N6 O2
Molecular Weight (MW) :	476.96
Lawson Number (LN) :	30824, 30355, 14903, 3018, 289
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7856774

Tautomer ID (TAUTID) : 8737736  
 Entry Date (DED) : 2003/04/17  
 Update Date (DUPD) : 2003/04/17



#### Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
LSF	Linearized Structure Formula	1
MF	Molecular Formula	1
FW	Formular Weight	1
FBRN	Fragment BRN	2
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
<hr/>		
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

Reaction:

RX

Reaction ID (.ID) : 9192198  
 Reactant BRN (.RBRN) : 9286129, 2831008  
 Reactant (.RCT) : 8-chloro-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile,  
                   4-chloro-5-methoxy-2-methyl-aniline  
 Product BRN (.PBRN) : 9303785  
 Product (.PRO) : 8-(4-chloro-5-methoxy-2-methyl-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 No. of React. Details (.NVAR) : 1

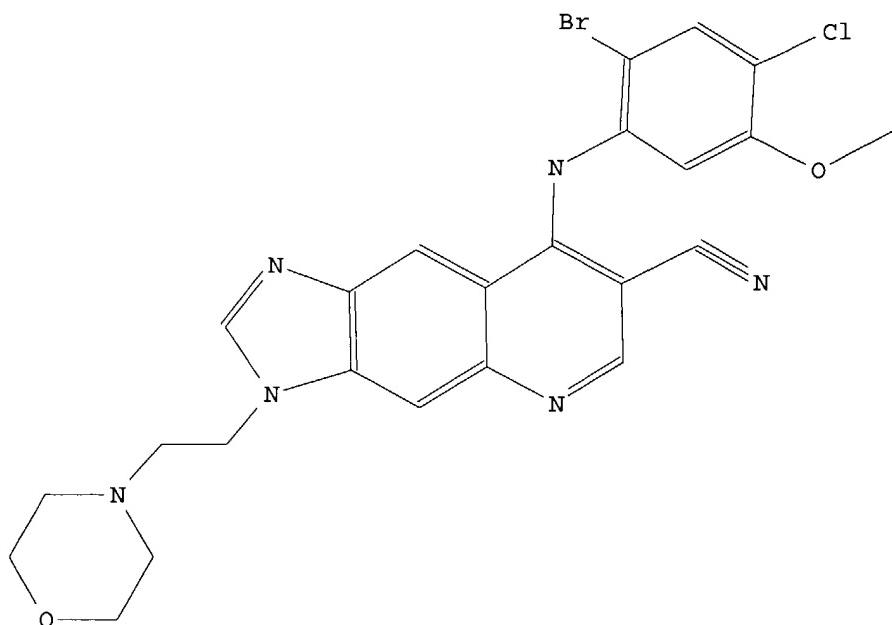
Reaction Details:

RX

Reaction RID (.RID) : 9192198.1  
 Reaction Classification (.CL) : Preparation  
 Reagent (.RGT) : pyridine hydrochloride  
 Solvent (.SOL) : 2-ethoxy-ethanol  
 Other Conditions (.COND) : Heating  
 Reference(s) :  
 1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan;  
    DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank,  
    Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766;  
    BABS-6374520

L17 ANSWER 5 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) : 9303647  
 Chemical Name (CN) : 8-(2-bromo-4-chloro-5-methoxy-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Autonom Name (AUN) : 8-(2-bromo-4-chloro-5-methoxy-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Molec. Formula (MF) : C24 H22 Br Cl N6 O2  
 Molecular Weight (MW) : 541.83  
 Lawson Number (LN) : 30824, 30355, 14894, 3018, 289  
 Compound Type (CTYPE) : heterocyclic  
 Constitution ID (CONSID) : 7856662  
 Tautomer ID (TAUTID) : 8737612  
 Entry Date (DED) : 2003/04/17  
 Update Date (DUPD) : 2003/04/17



## Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
<hr/>		
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

## Reaction:

RX

Reaction ID (.ID) :	9214177
Reactant BRN (.RBRN) :	9286129, 9044203
Reactant (.RCT) :	8-chloro-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile, 2-bromo-4-chloro-5-methoxy-phenylamine
Product BRN (.PBRN) :	9303647
Product (.PRO) :	8-(2-bromo-4-chloro-5-methoxy-phenylamino)- 3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-

g&gt;quinoline-7-carbonitrile

No. of React. Details (.NVAR) : 1

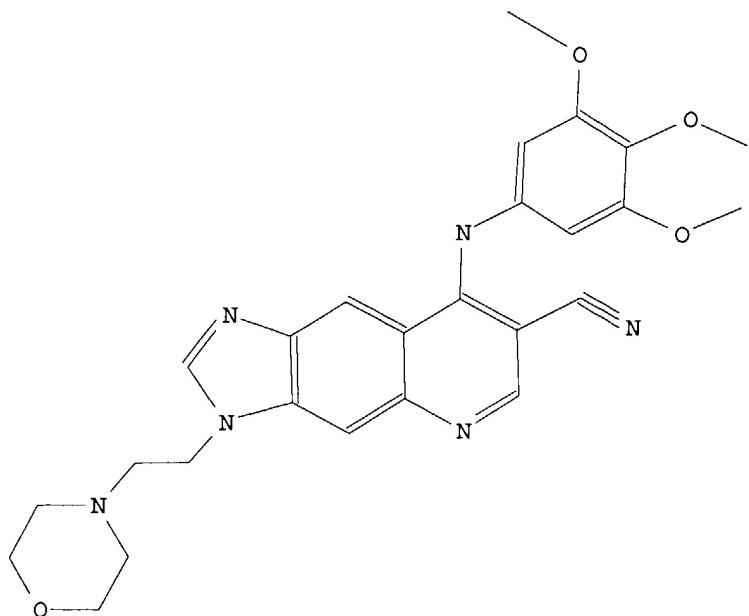
## Reaction Details:

RX

Reaction RID (.RID) : 9214177.1  
 Reaction Classification (.CL) : Preparation  
 Reagent (.RGT) : pyridine hydrochloride  
 Solvent (.SOL) : 2-ethoxy-ethanol  
 Other Conditions (.COND) : Heating  
 Reference(s) :  
 1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan;  
 DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank,  
*Bioorg.Med.Chem.Lett.*, CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766;  
 BABS-6374520

L17 ANSWER 6 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) : 9303524  
 Chemical Name (CN) : 3-(2-morpholin-4-yl-ethyl)-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Autonom Name (AUN) : 3-(2-morpholin-4-yl-ethyl)-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Molec. Formula (MF) : C26 H28 N6 O4  
 Molecular Weight (MW) : 488.55  
 Lawson Number (LN) : 30824, 30355, 15326, 3018, 289  
 Compound Type (CTYPE) : heterocyclic  
 Constitution ID (CONSID) : 7856543  
 Tautomer ID (TAUTID) : 8737585  
 Entry Date (DED) : 2003/04/17  
 Update Date (DUPD) : 2003/04/17



## Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
<hr/>		
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

## Reaction:

RX

Reaction ID (.ID) : 9208412  
 Reactant BRN (.RBRN) : 9286129, 642919  
 Reactant (.RCT) : 8-chloro-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile,  
                   3,4,5-trimethoxy-aniline  
 Product BRN (.PBRN) : 9303524  
 Product (.PRO) : 3-(2-morpholin-4-yl-ethyl)-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 No. of React. Details (.NVAR) : 1

## Reaction Details:

RX

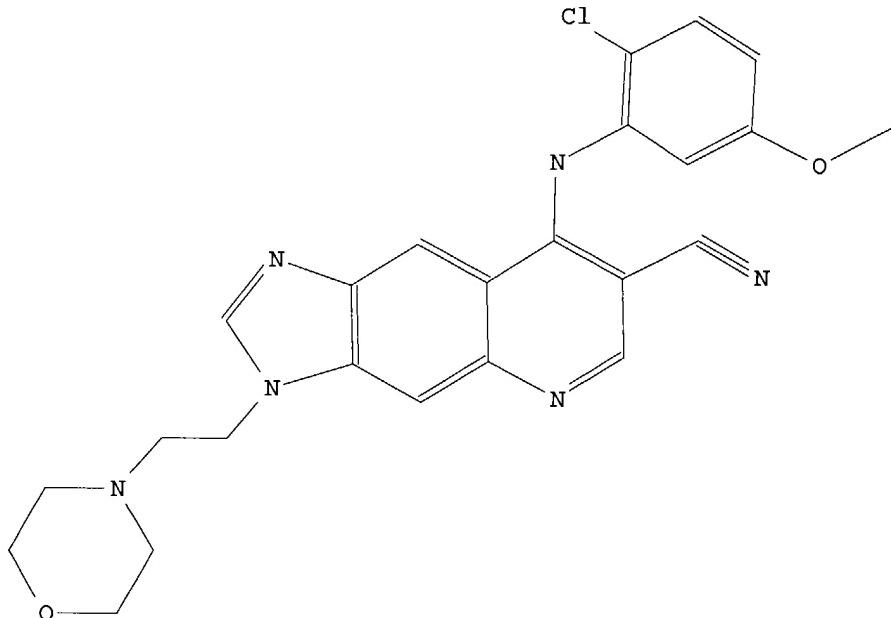
Reaction RID (.RID) : 9208412.1  
 Reaction Classification (.CL) : Preparation  
 Reagent (.RGT) : pyridine hydrochloride  
 Solvent (.SOL) : 2-ethoxy-ethanol  
 Other Conditions (.COND) : Heating  
 Reference(s) :  
 1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan;  
    DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank,  
    Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766;  
    BABS-6374520

L17 ANSWER 7 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) : 9301278  
 Chemical Name (CN) : 8-(2-chloro-5-methoxy-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Autonom Name (AUN) : 8-(2-chloro-5-methoxy-phenylamino)-3-(2-

Molec. Formula (MF) :  
 Molecular Weight (MW) :  
 Lawson Number (LN) :  
 Compound Type (CTYPE) :  
 Constitution ID (CONSID) :  
 Tautomer ID (TAUTID) :  
 Entry Date (DED) :  
 Update Date (DUPD) :

morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 C24 H23 Cl N6 O2  
 462.94  
 30824, 30355, 14893, 3018, 289  
 heterocyclic  
 7854680  
 8736936  
 2003/04/17  
 2003/04/17



#### Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
FBRN	Fragment BRN	2
LN	Lawson Number	5
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
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=====
RX      Reaction Documents          1
RXPRO   Substance is Reaction Product  1
```

## Reaction:

RX

Reaction ID (.ID) : 9190208  
 Reactant BRN (.RBRN) : 9286129, 2082193  
 Reactant (.RCT) : 8-chloro-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile,  
                   2-chloro-5-methoxy-aniline  
 Product BRN (.PBRN) : 9301278  
 Product (.PRO) : 8-(2-chloro-5-methoxy-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 No. of React. Details (.NVAR) : 1

## Reaction Details:

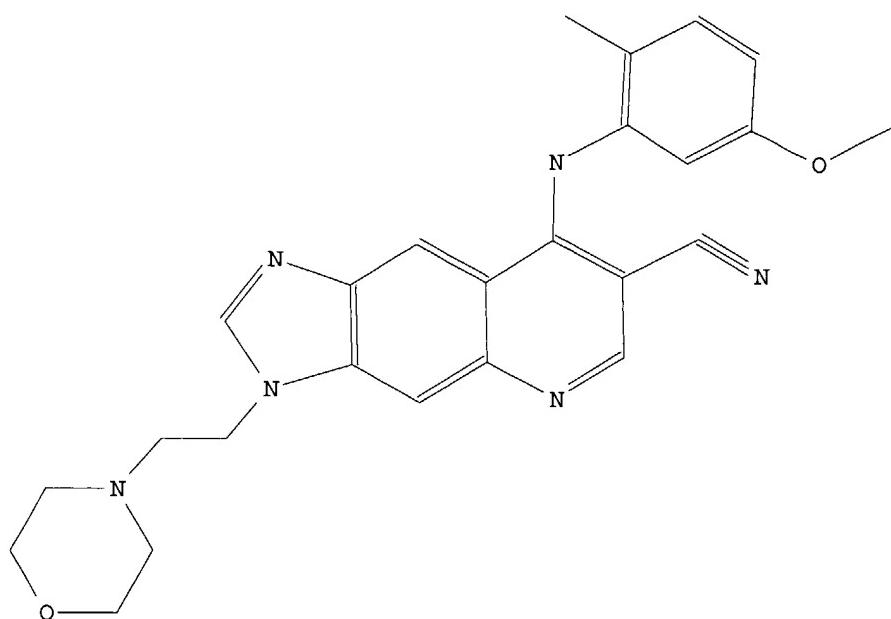
RX

Reaction RID (.RID) : 9190208.1  
 Reaction Classification (.CL) : Preparation  
 Reagent (.RGT) : pyridine hydrochloride  
 Solvent (.SOL) : 2-ethoxy-ethanol  
 Other Conditions (.COND) : Heating  
 Reference(s) :

1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520

L17 ANSWER 8 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9300518
Chemical Name (CN) :	8-(5-methoxy-2-methyl-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	8-(5-methoxy-2-methyl-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C25 H26 N6 O2
Molecular Weight (MW) :	442.52
Lawson Number (LN) :	30824, 30355, 14902, 3018, 289
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7854011
Tautomer ID (TAUTID) :	8737502
Entry Date (DED) :	2003/04/17
Update Date (DUPD) :	2003/04/17



## Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	5
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
<hr/>		
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

## Reaction:

RX

Reaction ID (.ID) :	9211265
Reactant BRN (.RBRN) :	9286129, 774678
Reactant (.RCT) :	8-chloro-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-g>quinoline-7-carbonitrile, 5-methoxy-2-methyl-aniline
Product BRN (.PBRN) :	9300518
Product (.PRO) :	8-(5-methoxy-2-methyl-phenylamino)-3-(2-morpholin-4-yl-ethyl)-3H-imidazo<4,5-

No. of React. Details (.NVAR) : 1  
 g>quinoline-7-carbonitrile

## Reaction Details:

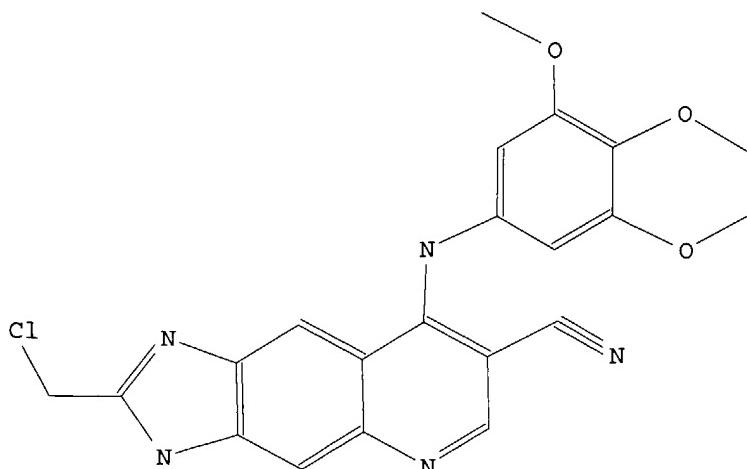
RX

Reaction RID (.RID) : 9211265.1  
 Reaction Classification (.CL) : Preparation  
 Reagent (.RGT) : pyridine hydrochloride  
 Solvent (.SOL) : 2-ethoxy-ethanol  
 Other Conditions (.COND) : Heating  
 Reference(s) :

1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520

L17 ANSWER 9 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) : 9297462  
 Chemical Name (CN) : 2-chloromethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Autonom Name (AUN) : 2-chloromethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 Molec. Formula (MF) : C21 H18 Cl N5 O3  
 Molecular Weight (MW) : 423.86  
 Lawson Number (LN) : 30357, 15326, 289  
 Compound Type (CTYPE) : heterocyclic  
 Constitution ID (CONSID) : 7851478  
 Tautomer ID (TAUTID) : 8728619  
 Entry Date (DED) : 2003/04/17  
 Update Date (DUPD) : 2003/04/17



## Field Availability:

Code	Name	Occurrence
------	------	------------

BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
FS	File Segment	1
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	2
RXREA	Substance is Reaction Reactant	1
RXPRO	Substance is Reaction Product	1

Reaction:

RX

Reaction ID (.ID) : 9205152  
 Reactant BRN (.RBRN) : 9294295, 605439  
 Reactant (.RCT) : 6,7-diamino-4-(3,4,5-trimethoxy-phenylamino)-quinoline-3-carbonitrile, chloroacetyl chloride  
 Product BRN (.PBRN) : 9297462  
 Product (.PRO) : 2-chloromethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 No. of React. Details (.NVAR) : 1

Reaction Details:

RX

Reaction RID (.RID) : 9205152.1  
 Reaction Classification (.CL) : Multistage  
 Nr. of Stages (.SNR) : 2  
 Stage 1  
 Reagent (.RGT) : Et2NPh  
 Stage 2  
 Reagent (.RGT) : acetic acid  
 Other Conditions (.COND) : Heating  
 Reference(s) :  
 1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg. Med. Chem. Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520

Reaction:

RX

Reaction ID (.ID) : 9177041  
 Reactant BRN (.RBRN) : 9297462, 102549  
 Reactant (.RCT) : 2-chloromethyl-8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile, morpholine  
 Product BRN (.PBRN) : 9304516  
 Product (.PRO) : 2-morpholin-4-ylmethyl-8-(3,4,5-trimethoxy-

phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile

No. of React. Details (.NVAR) : 1

**Reaction Details:**

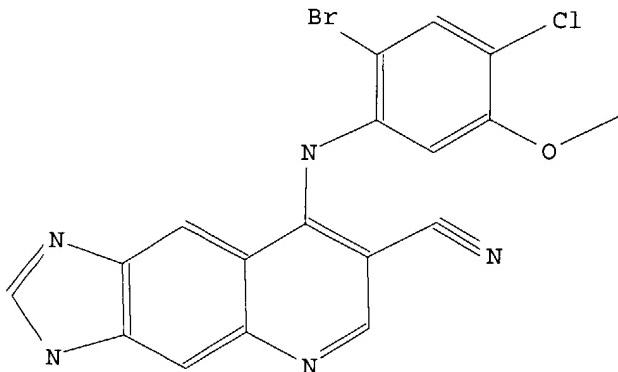
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Reaction RID (.RID) : 9177041.1  
 Reaction Classification (.CL) : Preparation  
 Reference(s) :

1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520

L17 ANSWER 10 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9292188
Chemical Name (CN) :	8-(2-bromo-4-chloro-5-methoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	8-(2-bromo-4-chloro-5-methoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C18 H11 Br Cl N5 O
Molecular Weight (MW) :	428.67
Lawson Number (LN) :	30355, 14894, 289
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7847049
Tautomer ID (TAUTID) :	8725288
Entry Date (DED) :	2003/04/17
Update Date (DUPD) :	2003/04/17



**Field Availability:**

Code	Name	Occurrence
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BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1

LN	Lawson Number	3
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

#### Reaction:

RX

Reaction ID (.ID) :	9214176
Reactant BRN (.RBRN) :	9266116, 9044203
Reactant (.RCT) :	8-chloro-3H-imidazo<4,5-g>quinoline-7-carbonitrile, 2-bromo-4-chloro-5-methoxy-phenylamine
Product BRN (.PBRN) :	9292188
Product (.PRO) :	8-(2-bromo-4-chloro-5-methoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
No. of React. Details (.NVAR) :	1

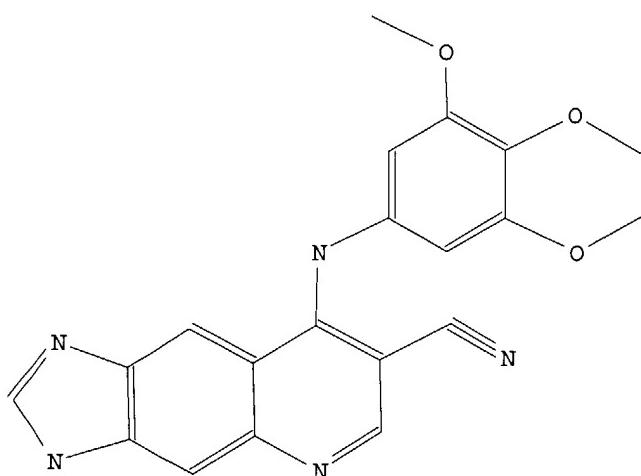
#### Reaction Details:

RX

Reaction RID (.RID) :	9214176.1
Reaction Classification (.CL) :	Preparation
Reagent (.RGT) :	pyridine hydrochloride
Solvent (.SOL) :	2-ethoxy-ethanol
Other Conditions (.COND) :	Heating
Reference(s) :	
1.	Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520

L17 ANSWER 11 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9291861
Chemical Name (CN) :	8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C20 H17 N5 O3
Molecular Weight (MW) :	375.39
Lawson Number (LN) :	30355, 15326, 289
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7846818
Tautomer ID (TAUTID) :	8725471
Entry Date (DED) :	2003/04/17
Update Date (DUPD) :	2003/04/17



## Field Availability:

Code	Name	Occurrence
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BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
NMR	Nuclear Magnetic Resonance	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
<hr/>		
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

## Reaction:

RX

Reaction ID (.ID): 9208408  
 Reactant BRN (.RBRN): 9266116, 642919  
 Reactant (.RCT): 8-chloro-3H-imidazo<4,5-g>quinoline-7-carbonitrile, 3,4,5-trimethoxy-aniline  
 Product BRN (.PBRN): 9291861  
 Product (.PRO): 8-(3,4,5-trimethoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 No. of React. Details (.NVAR): 1

## Reaction Details:

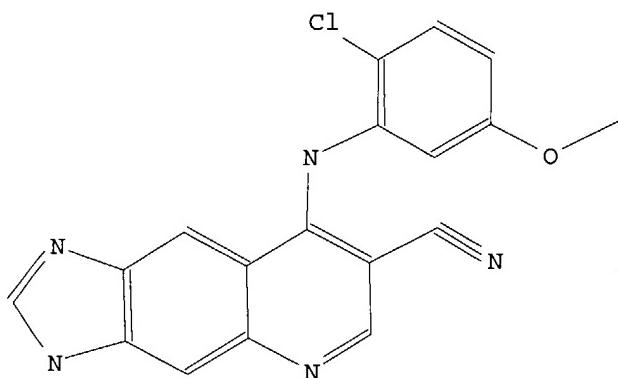
RX

Reaction RID (.RID): 9208408.1

Reaction Classification (.CL) : Preparation  
 Reagent (.RGT) : pyridine hydrochloride  
 Solvent (.SOL) : 2-ethoxy-ethanol  
 Other Conditions (.COND) : Heating  
 Reference(s) :  
 1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan;  
 DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank,  
 Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766;  
 BABS-6374520

L17 ANSWER 12 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9286966
Chemical Name (CN) :	8-(2-chloro-5-methoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	8-(2-chloro-5-methoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C18 H12 Cl N5 O
Molecular Weight (MW) :	349.78
Lawson Number (LN) :	30355, 14893, 289
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7842596
Tautomer ID (TAUTID) :	8723178
Entry Date (DED) :	2003/04/17
Update Date (DUPD) :	2003/04/17



Field Availability:

Code	Name	Occurrence
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BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	3
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1

ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

Reaction:

RX

Reaction ID (.ID) :	9190207
Reactant BRN (.RBRN) :	9266116, 2082193
Reactant (.RCT) :	8-chloro-3H-imidazo<4,5-g>quinoline-7-carbonitrile, 2-chloro-5-methoxy-aniline
Product BRN (.PBRN) :	9286966
Product (.PRO) :	8-(2-chloro-5-methoxy-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
No. of React. Details (.NVAR) :	1

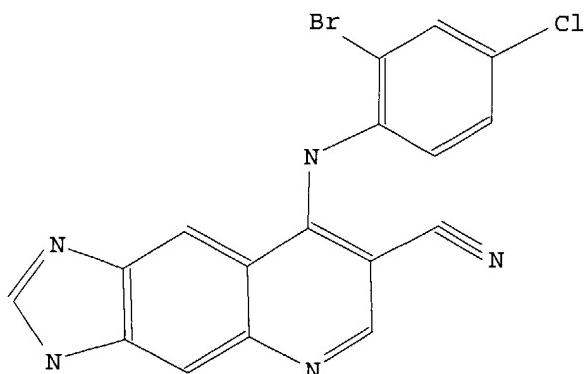
Reaction Details:

RX

Reaction RID (.RID) :	9190207.1
Reaction Classification (.CL) :	Preparation
Reagent (.RGT) :	pyridine hydrochloride
Solvent (.SOL) :	2-ethoxy-ethanol
Other Conditions (.COND) :	Heating
Reference(s) :	
1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg. Med. Chem. Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520	

L17 ANSWER 13 OF 13 BEILSTEIN COPYRIGHT 2004 BEILSTEIN MDL on STN

Beilstein Records (BRN) :	9286576
Chemical Name (CN) :	8-(2-bromo-4-chloro-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Autonom Name (AUN) :	8-(2-bromo-4-chloro-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile
Molec. Formula (MF) :	C17 H9 Br Cl N5
Molecular Weight (MW) :	398.65
Lawson Number (LN) :	30355, 14133
Compound Type (CTYPE) :	heterocyclic
Constitution ID (CONSID) :	7842299
Tautomer ID (TAUTID) :	8724399
Entry Date (DED) :	2003/04/17
Update Date (DUPD) :	2003/04/17



## Field Availability:

Code	Name	Occurrence
<hr/>		
BRN	Beilstein Records	1
CN	Chemical Name	1
AUN	Autonomname	1
MF	Molecular Formula	1
FW	Formular Weight	1
LN	Lawson Number	2
CTYPE	Compound Type	1
CONSID	Constitution ID	1
TAUTID	Tautomer ID	1
ED	Entry Date	1
UPD	Update Date	1
PHARM	Pharmacological Data	5

This substance also occurs in Reaction Documents:

Code	Name	Occurrence
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RX	Reaction Documents	1
RXPRO	Substance is Reaction Product	1

## Reaction:

RX

Reaction ID (.ID) : 9192082  
 Reactant BRN (.RBRN) : 9266116, 2802563  
 Reactant (.RCT) : 8-chloro-3H-imidazo<4,5-g>quinoline-7-carbonitrile, 2-bromo-4-chloro-aniline  
 Product BRN (.PBRN) : 9286576  
 Product (.PRO) : 8-(2-bromo-4-chloro-phenylamino)-3H-imidazo<4,5-g>quinoline-7-carbonitrile  
 No. of React. Details (.NVAR) : 1

## Reaction Details:

RX

Reaction RID (.RID) : 9192082.1  
 Reaction Classification (.CL) : Preparation  
 Reagent (.RGT) : pyridine hydrochloride  
 Solvent (.SOL) : 2-ethoxy-ethanol  
 Other Conditions (.COND) : Heating  
 Reference(s) :

1. Berger, Dan; Dutia, Minu; Powell, Dennis; Wu, Biqi; Wissner, Allan; DeMorin, Frenel; Weber, Jennifer; Boschelli, Frank, Bioorg.Med.Chem.Lett., CODEN: BMCLE8, 12(19), <2002>, 2761 - 2766; BABS-6374520

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FILE CONTENT: 1988-PRESENT (VOL 141 ISS 04) (20040723/ED)

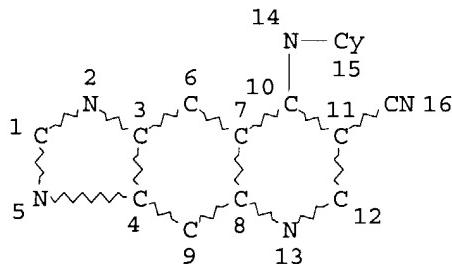
MOST RECENT CITATIONS FOR PATENTS FROM FIVE MAJOR ISSUING AGENCIES  
(COVERAGE TO THESE DATES IS NOT COMPLETE):

US	6747069	08 JUN 2004
DE	10351214	19 MAY 2004
EP	1424340	02 JUN 2004
JP	2004161736	10 JUN 2004
WO	2004052350	24 JUN 2004

Structure search limits have been raised. See HELP SLIMIT for the new, higher limits.

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L18 STR



#### NODE ATTRIBUTES:

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#### GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 16

#### STEREO ATTRIBUTES: NONE

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SEARCH TIME: 00.00.38

2 ANSWERS

=> d bib abs 120 tot ?

L20 ANSWER 1 OF 2 MARPAT COPYRIGHT 2004 ACS on STN  
AN 136:37618 MARPAT

\*TI Preparation of substituted aromatic tricyclic compounds containing nicotinonitrile rings as protein kinase inhibitors  
 IN Berger, Dan M.; Dutia, Minu D.; Demorin, Frenel F.; Boschelli, Diane H.; Powell, Dennis W.; Tsou, Hwei-ru; Wissner, Allan; Zhang, Nan; Ye, Fei; Wu, Biqi

PA American Home Products Corporation, USA; Wyeth

SO U.S. Pat. Appl. Publ., 107 pp.

CODEN: USXXCO

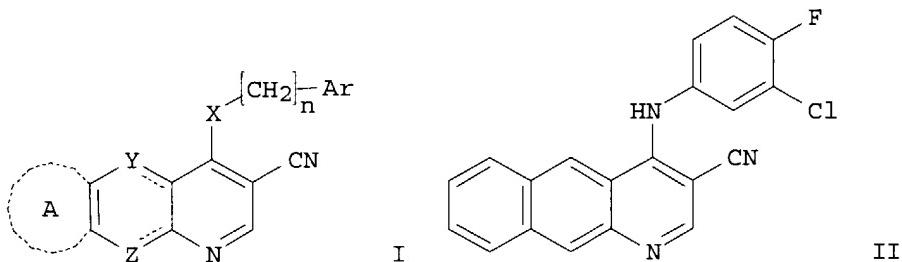
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001051620	A1	20011213	US 2000-751274	20001229
	US 6638929	B2	20031028		
	US 2004110762	A1	20040610	US 2003-618044	20030710
PRAI	US 1999-240905P	19991229			
	US 2000-751274	20001229			

GI



AB The title compds. I [Ar = (un)substituted cycloalkyl, pyridyl, pyrimidinyl, etc.; n = 0-1; X = NH, O, S, NR; R = alkyl; Y, Z = both carbon or N; A = (un)substituted benzo, pyrido, pyrimido, etc.] which are useful as inhibitors of protein tyrosine kinase and are antiproliferative agents, were prepared E.g., a 3-step synthesis of II which showed IC50 of 0.005 .mu.M against EGF-R kinase (recombinant enzyme), was given.

L20 ANSWER 2 OF 2 MARPAT COPYRIGHT 2004 ACS on STN

AN 135:92639 MARPAT

\*TI Preparation of substituted aromatic tricyclic compounds containing nicotinonitrile rings as protein kinase inhibitors

IN Berger, Dan M.; Dutia, Minu D.; Demorin, Frenel F.; Boschelli, Diane H.; Powell, Dennis W.; Tsou, Hwei-ru; Wissner, Allan; Zhang, Nan; Ye, Fei; Wu, Biqi

PA American Home Products Corp., USA

SO PCT Int. Appl., 377 pp.

CODEN: PIXXD2

DT Patent

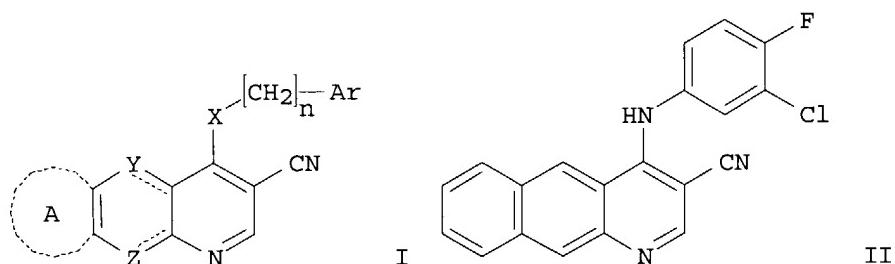
LA English

FAN.CNT 1

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PI	WO 2001047892	A1	20010705	WO 2000-US35616	20001229	
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SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,  
 ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1242382 A1 20020925 EP 2000-988437 20001229  
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 BR 2000016878 A 20021008 BR 2000-16878 20001229  
 JP 2003519127 T2 20030617 JP 2001-549364 20001229  
 PRAI US 1999-473600 19991229  
 WO 2000-US35616 20001229

GI



AB The title compds. I [Ar = (un)substituted cycloalkyl, pyridyl, pyrimidinyl, etc.; n = 0-1; X = NH, O, S, NR; R = alkyl; Y, Z = both carbon or N; A = (un)substituted benzo, pyrido, pyrimido, etc.] which are useful as inhibitors of protein tyrosine kinase and are antiproliferative agents, were prepared E.g., a 3-step synthesis of II which showed IC50 of 0.005 .mu.M against EGF-R kinase (recombinant enzyme), was given.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

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